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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GUSSOW, ANNE

ART UNIT

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1643

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/540,539	<b>Applicant(s)</b> ZHOU ET AL.	
	<b>Examiner</b> Anne M. Gussow	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 February 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-14 and 17-23 is/are pending in the application.
- 4a) Of the above claim(s) 7-11,14 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,6,12,13,22 and 23 is/are rejected.
- 7) ☒ Claim(s) 5 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/12/10</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignment</u> .               |

### **DETAILED ACTION**

1. Claims 1, 2, 5, 6, 12, and 13 have been amended.

Claims 3, 4, 15, and 16 have been cancelled.

Claims 22 and 23 have been added.

Claims 7-11, 14, and 17-21 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 13, 2007.

2. Claims 1, 2, 5, 6, 12, 13, 22, and 23 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

### ***Information Disclosure Statement***

4. The information disclosure statement (IDS) submitted on February 12, 2010 was filed after the mailing date of the non-final rejection on September 1, 2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

***Objections Withdrawn***

5. The objection to claims 12 and 13 is withdrawn in view of applicant's amendment to the claims.

***Rejections Withdrawn***

6. The rejection of claims 1, 2, 3, 6, 12, and 13 under 35 U.S.C. 112, first paragraph as lacking enablement is withdrawn in view of applicant's amendment to the claims.
7. The rejection of claim 13 under 35 U.S.C. 101 as being directed to non-statutory subject matter is withdrawn in view of applicant's amendment to the claim.

***NEW GROUNDS of Rejection***

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a transfected, mutated and isolated cell line. The specification discloses a cell line transfected with an expression vector comprising the nucleotide sequence of SEQ ID Nos. 1 or 6. The specification does not describe

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mutated cell lines. It is not clear what is mutated in the cell line. It is not clear what the purpose of the mutation in the cell line would be.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cancer related nucleotide sequences of SEQ ID Nos. 1 and 6 and the cancer related polypeptide sequence of SEQ ID No. 4, does not reasonably provide enablement for all of the possible cancer related nucleotide sequences encoding SEQ ID No. 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,  
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to all possible cancer related nucleotide sequences that encode SEQ ID No. 4.

The specification discloses the nucleotide sequence of SEQ ID No. 1 encodes SEQ ID No. 4 and is overexpressed in cancer. The specification does not disclose other degenerate nucleotide sequences which would encode SEQ ID No. 4 are associated with cancer. One of ordinary skill in the art would be forced into undue experimentation to determine which of the degenerate nucleotide sequence which encode SEQ ID No. 4 would be cancer related.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess, et al., Journal of Cell Biology, 1990. Vol. 111, pages 2129-2138, as cited in the office action mailed November 13, 2007). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar, et al. Molecular and Cellular Biology, 1988. Vol. 8 pages 1247-1252, as cited in the office action mailed November 13, 2007).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz, et al., Proceedings of the National Academy of Sciences, 1987. Vol. 84, pages 6408-6411, as cited in the office action mailed

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November 13, 2007). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin, et al. Biochemistry, 1975. Vol. 14, pages 1559-1563 as cited in the office action mailed November 13, 2007).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting synthetic DNA sequence. For example, the cellular location of the Int-2 oncoprotein is determined by the choice of initiation codon, i.e., either the AUG coding for methionine or CUG coding for leucine. AUG-initiated Int-2 proteins are secreted from the cells, while CUG-initiated Int-2 proteins are localized to the cell nucleus (Acland, et al., Nature 1990. Vol. 343, pages 662-665).

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation of the genetic code induces one to believe that one can readily obtain a functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as Burgess, et al., Lazar, et al., Schwartz, et al., Lin, et al. and Acland, et al. conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed

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in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 2, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Shao and Zhou (Accession Number AY057051, first submitted September 24, 2001).

The claims recite a human cancer-related isolated polynucleotide sequence, comprising one of the following nucleotide sequences: SEQ ID No: 1 or SEQ ID No: 6 in the sequence listings, wherein said human cancers are selected from liver cancer, lung cancer, stomach cancer, colon cancer, and breast cancer.

Shao and Zhou teach the mRNA sequence of SEQ ID No. 1 (see sequence alignment) isolated from hepatocellular carcinoma, which is a form a liver cancer. Since the sequence of Shao and Zhou is identical to the instant SEQ ID No. 1 and was isolated from liver cancer all the limitations of the claims have been met.

14. Claims 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Wiemann, et al (Genome Research, 2001. Vol. 11, pages 422-435).

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The claims recite a human cancer-related isolated polynucleotide sequence, comprising a nucleotide sequence encoding, SEQ ID No: 4 in the sequence listings, wherein the said human cancers are selected from liver cancer, lung cancer, stomach cancer, colon cancer, and breast cancer.

Wiemann, et al. teach the nucleotide sequence (note isoform 3 of the sequence alignment) encoding a polypeptide that is identical to SEQ ID No. 4 (see sequence alignment). The gene information for LAP4B identifies SEQ ID No. 4 as cancer related (see sequence alignment). Since the sequence of Wiemann, et al. is identical to the instant SEQ ID No. 4 all the limitations of the claims have been met.

### ***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1, 2, 6, 12, and 13 are rejected under 35 U.S.C. 103(a) as being obvious over Shao and Zhou (Accession Number AY057051, first submitted September 24, 2001) in view of Nakamura, et al. (US PG PUB 2005/0259483, priority to September 30, 2002).

Claims 1, 2 and 6 have been described supra. Claims 12 and 13 recite an expression vector comprising the human cancer- related isolated polynucleotide sequence according to claim 1. A transfected, mutated and purified cell lines comprising the human cancer-related isolated polynucleotide sequence according to claim 1.

Shao and Zhou have been described supra. Shao and Zhou do not teach the nucleotide sequence in a vector or host cell. This deficiency is made up for in the teachings of Nakamura, et al.

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Nakamura, et al. teach the expression of cancer related polypeptides in expression vectors and host cells (see paragraphs 58, 66, and 82-88).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have expressed the nucleotide sequence of Shao and Zhou in the expression vector and host cell as taught by Nakamura, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have expressed the nucleotide sequence of Shao and Zhou in the expression vector and host cell as taught by Nakamura, et al. because Nakamura, et al. teach expression vectors and host cells for the purpose of expressing cancer related sequences. Further, Nakamura, et al. teach the expression vectors for the production of cancer related polypeptides for use in cancer therapy. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the nucleotide sequence of Shao and Zhou for expression in an expression vector and host cell in view of Nakamura, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

### ***Conclusion***

19. Claims 1, 2, 6, 12, 13, 22, and 23 are rejected.

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Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow  
April 15, 2010

/Anne M. Gussow/  
Examiner, Art Unit 1643